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Scientific and Technical Information Center
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SEARCH REQUEST FORM

Date: 12/2/99 Requester's Full Name: DAVID LUKTON Examiner #: 71263
Art Unit: 1654 Phone (308) 3213 Serial Number: 09/126958
Results Format Preferred (circle): PAPER DISK E-MAIL

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To ensure an efficient and quality search, please attach a copy of the cover sheet, claims, and abstract or fill out the following:

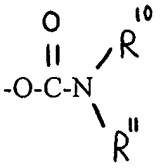
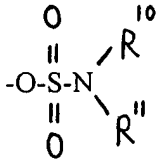
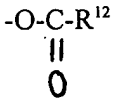
TITLE: CARBAMYLOXY COMPOUNDS WHICH INHIBIT LEUKOCYTE ADHESION MEDIATED BY VLA-4

INVENTORS: (A) THORSETT,EUGENE D; (B) SEMKO,CHRISTOPHER M. (C) SARANTAKIS, DIMITRIOS; (D) PLEISS,MICHAEL A. (E) KREFT,ANTHONY (F) KONRADI, ANDREI W. (G) GRANT,FRANCINE S. (H) DRESSEN,DARREN B.; (I) ASHWELL,SUSAN (J) BAUDY, REINHARDT BERNHARD (K) LOMBARDO,LOUIS JOHN

Priority Date: 7/31/97

Applicants are claiming the compounds on the attached sheet. The variables are as follows:

R^1 = anything;
R^6 = anything;
R^8 = anything;
R^9 = anything;
Ar = aryl or heteroaryl;
n = 1 or 2;
x = 1 or 2;

R^5 =  or  or 

wherein R^{10} and R^{11} can be anything;
R^{12} is any heterocyclic group;

****

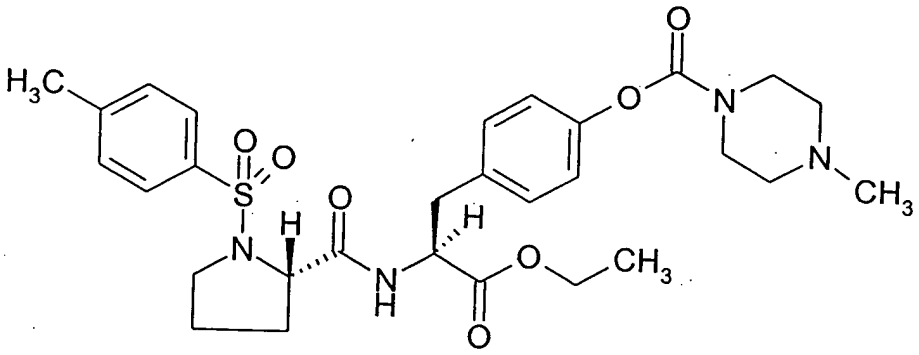
STAFF USE ONLY
Searcher: Sheppard
Searcher Phone #: 308-4499
Searcher Location:
Date Searcher Picked Up:
Date Completed: 12/8/99
Searcher Prep & Review Time:
Online Time:

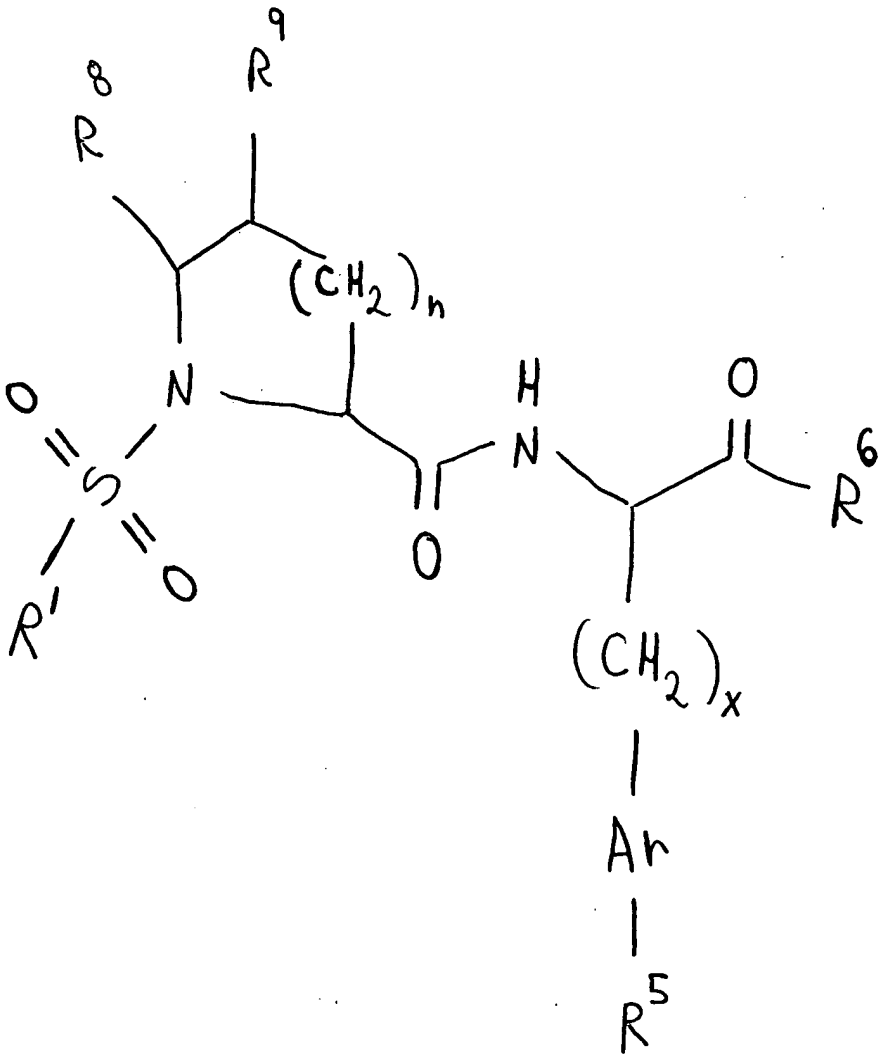
Type of Search
NA Sequence (#)
AA Sequence (#)
1 Structure (#)
Bibliographic
Litigation
Fulltext
Other

Vendors and Cost
STN Dialog
Questel/Orbit Dr.Link
Lexis/Nexis Westlaw
WWW/Internet
In-house sequence systems (list)
Other (specify)

09/126,958

Example of a claimed compound:





=> fil hcaplus

FILE 'HCAPLUS' ENTERED AT 15:10:54 ON 08 DEC 1999
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FILE COVERS 1967 - 8 Dec 1999 VOL 131 ISS 24
FILE LAST UPDATED: 7 Dec 1999 (19991207/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

This file supports REG1stRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

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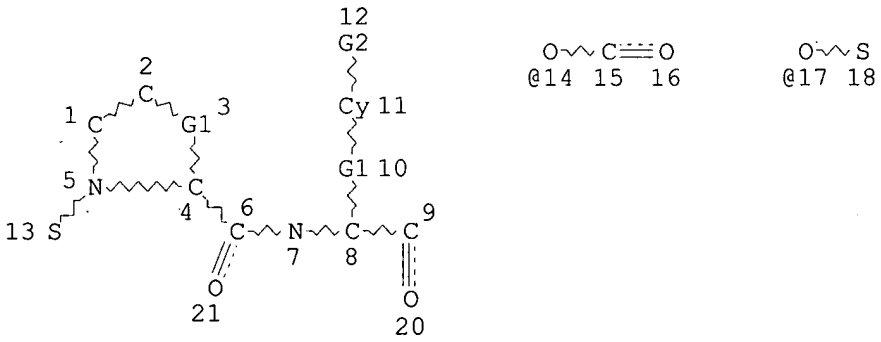
L1 STR



REP G1=(0-1) C
VAR G2=14/17
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 20

STEREO ATTRIBUTES: NONE
L3 214 SEA FILE=REGISTRY SSS FUL L1
L4 5 SEA FILE=HCAPLUS ABB=ON PLU=ON L3

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=> d ibib abs hitrn l4 1-5

L4 ANSWER 1 OF 5 HCAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1999:113712 HCAPLUS
DOCUMENT NUMBER: 130:168662
TITLE: Preparation of N-sulfonylproline dipeptide derivatives and analogs as inhibitors of leukocyte adhesion mediated by VLA-4
INVENTOR(S): Thorsett, Eugene D.; Semko, Christopher M.; Pleiss, Michael A.; Kreft, Anthony; Konradi, Andrei W.; Grant, Francine S.; Baudy, Reinhardt Bernhard; Sarantakis, Dimitrios
PATENT ASSIGNEE(S): Athena Neurosciences, Inc., USA; American Home Products Corporation
SOURCE: PCT Int. Appl., 294 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9906437	A1	19990211	WO 1998-US16070	19980731
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9888234	A1	19990222	AU 1998-88234	19980731
PRIORITY APPLN. INFO.:			US 1997-904423	19970731
			WO 1998-US16070	19980731

OTHER SOURCE(S): MARPAT 130:168662

AB Disclosed are title compds. R1SO2NR2CHR3QCHR5COR6 [R1 = (un)substituted alkyl, (un)substituted aryl, (un)substituted cycloalkyl, (un)substituted heterocyclyl; R2 = H, any group R1; R1R2 may form (un)substituted heterocyclic ring; R3 = H, any group R1; R2R3 may form (un)substituted heterocyclic ring; R5 = CH2X1; X1 = H, OH, acylamino, (un)substituted alkyl, alkoxy, aryloxy, aryl, aryloxyaryl, CO2H, carboxyalkyl, carboxyaryl, carboxyheteroaryl, (un)substituted cycloalkyl, (un)substituted heterocyclyl; Q = C(X)NR7; R7 = H, alkyl; X = O, S; R6 = NH2, (un)substituted alkoxy, (un)substituted cycloalkoxy, succinimidyloxy, adamantylamino, .beta.-cholest-5-en-3-yloxy, NHOY, NH(CH2)pCO2Y, OCH2NR9R10; Y = H, (un)substituted alkyl, (un)substituted aryl; p = 1-8; R9 = (un)substituted CO-aryl; R10 = H, CH2CO2R11, NHSO2Z'; R11 = alkyl; Z' = (un)substituted alkyl, (un)substituted cycloalkyl, (un)substituted aryl, (un)substituted heteroaryl, (un)substituted heterocyclyl; and pharmaceutically acceptable salts thereof, with provisos] which bind VLA-4 (also referred to as integrin .alpha.4.beta.1 and CD49d/CD29). Certain of these compds. also inhibit leukocyte adhesion and, in particular, leukocyte adhesion mediated by VLA-4. Such compds. are useful in the treatment of inflammatory diseases in a mammalian patient, e.g., human, wherein the disease may be, for example, asthma, Alzheimer's disease, atherosclerosis, AIDS dementia, diabetes, inflammatory bowel disease, rheumatoid arthritis, tissue transplantation, tumor metastasis and myocardial ischemia. The compds. can also be administered for the treatment of inflammatory brain diseases such as multiple sclerosis. Thus, BOP-mediated peptide coupling of Ts-Pro-OH (Ts = tosyl) with H-Tyr-OMe gave 75% of the corresponding ester, which underwent sapon. in quant. yield to give desired dipeptide Ts-Pro-Tyr-OH. All prepd. compds. have IC50 .ltoreq. 15 .mu.M in a VLA-4 binding assay.

IT **220303-19-5P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP

(Preparation); USES (Uses)
(prepn. of N-sulfonylproline dipeptide derivs. and analogs as inhibitors of leukocyte adhesion mediated by VLA-4)

L4 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1999:113710 HCAPLUS
DOCUMENT NUMBER: 130:153984
TITLE: Preparation of N-sulfonyl dipeptide derivatives and analogs as inhibitors of leukocyte adhesion mediated by VLA-4
INVENTOR(S): Thorsett, Eugene D.; Semko, Christopher M.; Pleiss, Michael A.; Konradi, Andrei W.; Grant, Francine S.; Dressen, Darren B.; Baudy, Reinhardt Bernhard
PATENT ASSIGNEE(S): Athena Neurosciences, Inc., USA; American Home Products Corporation
SOURCE: PCT Int. Appl., 151 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9906435	A1	19990211	WO 1998-US15314	19980730
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9886612	A1	19990222	AU 1998-86612	19980730
PRIORITY APPLN. INFO.:			US 1997-904415	19970731
			WO 1998-US15314	19980730

OTHER SOURCE(S): MARPAT 130:153984

AB Disclosed are title compds. R1SO2NR2CR3R4QCHR5COR6 [R1 = (un)substituted alkyl, (un)substituted aryl, (un)substituted cycloalkyl, (un)substituted heterocyclyl; R2 = H, any group R1, (un)substituted cycloalkenyl; R1R2 may form heterocyclic ring; R3 = any group R1; R2R3 may form heterocyclic ring; R4 = any group R1; R3R4 may form cycloalkyl, (un)substituted heterocyclic ring; R5 = CHMe2, CH2X, :CHX1; X1 = H, OH, acylamino, optionally substituted alkyl, alkoxy, aryloxy, aryl, aryloxyaryl, carboxy, carboxyalkyl, etc.; Q = C(X)NR7, X = O, S, R7 = H, alkyl; X = O, S; R6 = NH2, (un)substituted alkoxy, (un)substituted cycloalkoxy, succinimidyloxy, adamantylamino, .beta.-cholest-5-en-3-yloxy, NHOY, NH(CH2)pCO2Y, OCH2NR9R10; Y = H, (un)substituted alkyl, (un)substituted aryl; p = 1-8; R9 = (un)substituted CO-aryl; R10 = H, CH2CO2R11, NHSO2Z; R11 = alkyl; Z = (un)substituted alkyl, (un)substituted cycloalkyl, (un)substituted aryl, (un)substituted heteroaryl, (un)substituted heterocyclyl; and pharmaceutically acceptable salts thereof, with provisos] which bind VLA-4 (also referred to as integrin .alpha.4.beta.1 and CD49d/CD29). Certain of these compds. also inhibit leukocyte adhesion and, in particular, leukocyte adhesion mediated by VLA-4. Such compds. are useful in the treatment of inflammatory diseases in a mammalian patient, e.g., human, wherein the disease may be, for example, asthma, Alzheimer's disease, atherosclerosis, AIDS dementia, diabetes, inflammatory bowel disease, rheumatoid arthritis, tissue transplantation, tumor metastasis and myocardial ischemia. The compds. can also be administered for the treatment of inflammatory brain diseases such as multiple sclerosis. Thus, sulfonylation of cycloleucine (1-aminocyclopentanecarboxylic acid) with tosyl chloride, followed by peptide coupling with L-phenylalanine Me ester and sapon. gave desired title compd. 4-MeC6H4SO2-cycloleucyl-L-phenylalanine.

IT **220172-88-3P 220172-90-7P**

RL: BAC (Biological activity or effector, except adverse); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of N-sulfonyl dipeptide derivs. and analogs as inhibitors of leukocyte adhesion mediated by VLA-4)

IT **220172-89-4P 220172-92-9P 220173-39-7P**
220173-40-0P 220173-41-1P 220173-42-2P
220173-43-3P 220173-45-5P 220173-47-7P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of N-sulfonyl dipeptide derivs. and analogs as inhibitors of leukocyte adhesion mediated by VLA-4)

L4 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1999:113667 HCAPLUS
DOCUMENT NUMBER: 130:177528
TITLE: .alpha.9-Integrin antagonists and anti-inflammatory compositions
INVENTOR(S): Yednock, Theodore A.; Pleiss, Michael A.
PATENT ASSIGNEE(S): Athena Neurosciences, Inc., USA
SOURCE: PCT Int. Appl., 60 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9906391	A1	19990211	WO 1998-US15958	19980731
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9886050	A1	19990222	AU 1998-86050	19980731
EP 954519	A1	19991110	EP 1998-937310	19980731
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
PRIORITY APPLN. INFO.:			US 1997-904424	19970731
			US 1997-54453	19970801
			WO 1998-US15958	19980731

OTHER SOURCE(S): MARPAT 130:177528

AB Pharmaceutical compns. and methods are provided for treating inflammatory conditions, particularly those that are characterized by increased binding of .alpha.9-integrin to one or more of its ligands. Also disclosed are methods for selecting compds. for use in such compns. and methods.

IT **220543-91-9P 220543-92-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction; .alpha.9-integrin antagonists and anti-inflammatory compns.)

IT **220543-95-3 220543-99-7 220544-50-3**
220545-11-9
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(.alpha.9-integrin antagonists and anti-inflammatory compns.)

IT **220543-93-1P 220543-94-2P 220605-30-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(.alpha.9-integrin antagonists and anti-inflammatory compns.)

L4 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1999:113666 HCAPLUS

DOCUMENT NUMBER: 130:182768
TITLE: Preparation of N-sulfonyl O-carbamoyltyrosine dipeptide derivatives and analogs as inhibitors of leukocyte adhesion mediated by VLA-4
INVENTOR(S): Thorsett, Eugene D.; Semko, Christopher M.; Sarantakis, Dimitrios; Pleiss, Michael A.; Kreft, Anthony; Konradi, Andrei W.; Grant, Francine S.; Dressen, Darren B.; Ashwell, Susan; Baudy, Reinhardt Bernhard; Lombardo, Louis John
PATENT ASSIGNEE(S): Athena Neurosciences, Inc., USA; American Home Products Corporation
SOURCE: PCT Int. Appl., 386 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9906390	A1	19990211	WO 1998-US15324	19980731
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9885849	A1	19990222	AU 1998-85849	19980731
PRIORITY APPLN. INFO.:			US 1997-904424	19970731
			US 1997-54453	19970801
			WO 1998-US15324	19980731

OTHER SOURCE(S): MARPAT 130:182768

AB Disclosed are title compds. R1SO2NR2CHR3QCHR5COR6 [R1 = (un)substituted alkyl, (un)substituted aryl, (un)substituted cycloalkyl, (un)substituted heterocyclyl; R2 = H, any group R1; R1R2 may form (un)substituted heterocyclic ring; R3 = H, any group R1; R2R3 may form (un)substituted heterocyclic ring; R5 = (CH2)x-Ar-R5'; R5' = OZNR8R8', OZR12; R8, R8' = independently H, (un)substituted alkyl, (un)substituted cycloalkyl, (un)substituted heterocyclyl; R12 = (un)substituted heterocyclyl; Z = CO, SO2; Ar = (un)substituted aryl or heteroaryl; x = 1-4; Q = C(X)NR7; R7 = H, alkyl; X = O, S; R6 = NH2, (un)substituted alkoxy, (un)substituted cycloalkoxy, succinimidyloxy, adamantylamino, .beta.-cholest-5-en-3-yloxy, NHOY, NH(CH2)pCO2Y, OCH2NR9R10; Y = H, (un)substituted alkyl, (un)substituted aryl; p = 1-8; R9 = (un)substituted CO-aryl; R10 = H, CH2CO2R11, NHSO2Z'; R11 = alkyl; Z' = (un)substituted alkyl, (un)substituted cycloalkyl, (un)substituted aryl, (un)substituted heteroaryl, (un)substituted heterocyclyl; and pharmaceutically acceptable salts thereof, with provisos] which bind VLA-4 (also referred to as integrin .alpha.4.beta.1 and CD49d/CD29). Certain of these compds. also inhibit leukocyte adhesion and, in particular, leukocyte adhesion mediated by VLA-4. Such compds. are useful in the treatment of inflammatory diseases in a mammalian patient, e.g., human, wherein the disease may be, for example, asthma, Alzheimer's disease, atherosclerosis, AIDS dementia, diabetes, inflammatory bowel disease, rheumatoid arthritis, tissue transplantation, tumor metastasis and myocardial ischemia. The compds. can also be administered for the treatment of inflammatory brain diseases such as multiple sclerosis. Thus, carbamoylation of Ts-Pro-Tyr-OEt (Ts = tosyl) with Me2NCOCl in the presence of Et3N and DMAP gave 99% desired title compd. Ts-Pro-Tyr(CONMe2)-OEt (I). Sapon. of I gave the corresponding free acid Ts-Pro-Tyr(CONMe2)-OH. All prepd. compds. have IC50 .ltoreq. 15 .mu.M in a VLA-4 binding assay.

IT **220543-91-9P 220543-92-0P 220543-99-7P**
220544-11-6P 220544-18-3P 220544-27-4P
220544-46-7P 220544-48-9P 220544-64-9P

220544-65-0P 220544-66-1P 220544-67-2P
220544-70-7P 220544-71-8P 220544-80-9P
220544-90-1P 220544-92-3P 220544-94-5P
220545-05-1P 220545-12-0P 220545-14-2P
220545-15-3P 220545-26-6P 220545-36-8P
220545-37-9P 220545-39-1P 220545-49-3P
220545-51-7P 220545-52-8P 220545-53-9P
220545-71-1P 220545-77-7P 220545-93-7P
220546-37-2P 220546-55-4P 220546-68-9P
220546-81-6P 220546-84-9P 220546-90-7P
220546-94-1P 220546-96-3P 220546-98-5P
220547-04-6P 220547-06-8P 220547-98-8P
RL: BAC (Biological activity or effector, except adverse); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of N-sulfonyl O-carbamoyltyrosine dipeptide derivs. and analogs as inhibitors of leukocyte adhesion mediated by VLA-4)

IT 220543-93-1P 220543-94-2P 220543-95-3P
220543-96-4P 220543-97-5P 220543-98-6P
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220544-33-2P 220544-34-3P 220544-35-4P
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220545-95-9P 220546-38-3P 220546-41-8P
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220546-58-7P 220546-59-8P 220546-60-1P
220546-61-2P 220546-62-3P 220546-70-3P
220546-78-1P 220546-82-7P 220546-83-8P
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220546-89-4P 220546-91-8P 220546-92-9P
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220547-55-7P 220547-57-9P 220547-58-0P
220547-59-1P 220547-60-4P 220547-61-5P
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RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP

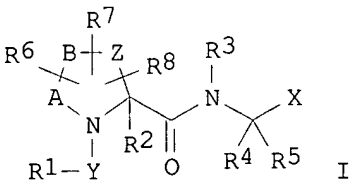
(Preparation); USES (Uses)
(prepn. of N-sulfonyl O-carbamoyltyrosine dipeptide derivs. and analogs as inhibitors of leukocyte adhesion mediated by VLA-4)

IT **220548-09-4**
RL: RCT (Reactant)
(prepn. of N-sulfonyl O-carbamoyltyrosine dipeptide derivs. and analogs as inhibitors of leukocyte adhesion mediated by VLA-4)

L4 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1998:799992 HCAPLUS
DOCUMENT NUMBER: 130:52724
TITLE: Preparation of heterocyclic dipeptide derivatives as cell adhesion inhibitors
INVENTOR(S): Durette, Philippe L.; Hagmann, William K.; Maccoss, Malcolm; Mills, Sander G.; Mumford, Richard A.; Van Riper, Gail M.; Schmidt, Jack A.; Kevin, Nancy J.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 129 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9853814	A1	19981203	WO 1998-US10940	19980529
W: CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
PRIORITY APPLN. INFO.:			US 1997-48017	19970529
			GB 1997-14314	19970707
			US 1997-66525	19971125
			GB 1998-686	19980114

OTHER SOURCE(S): MARPAT 130:52724
GI



I

AB Title compds. I [R1 = (un)substituted C1-10 alkyl, C2-10 alkenyl, C2-10 alkynyl, Cy, Cy-C1-10 alkyl, Cy-C2-10 alkenyl, Cy-C2-10 alkynyl; R2, R5 = independently (un)substituted H, C1-10 alkyl, C2-10 alkenyl, C2-10 alkynyl, aryl, aryl-C1-10 alkyl, heteroaryl, heteroaryl-C1-10 alkyl; R3 = H, (un)substituted C1-10 alkyl, Cy, Cy-C1-10 alkyl; R4 = H, any group R1; R3R4 form mono- or bicyclic ring contg. 0-2 heteroatoms N, O, S; R4R5 form 3-7 membered mono- or bicyclic ring contg. 0-2 heteroatoms N, O, S; R10, R11 = independently = any group R3, (un)substituted C2-10 alkenyl, C2-10 alkynyl; R10R11 may form 5-7 membered heterocyclic ring contg. 0-2 addnl. heteroatoms N, O, S; R6-R8 = independently any group R10, OR10, NO2, halo, S(O)mR10, SR10, SO3R10, NR10R11, COR10, CO2R10, O2R10, CN, CONR10R11, CF3, oxo, NR10S(O)mR11, etc.; two of R6-R8 may form 5-7 membered (un)satd. monocyclic ring contg. 0-3 heteroatoms N, O, S; Cy = cycloalkyl, heterocyclyl, aryl, heteroaryl; A, Z = independently C, C-C; B = bond, C, C-C, N, O, S, S(O)m; X = CO2R10, P(O)(OR10)(OR11), P(O)(R10)(OR11), S(O)mOR10, CONR10R11, 5-tetrazolyl; Y = CO, O2C, NR11CO, SO2, P(O)(OR4), COCO; m = 1-2] = are antagonists of VLA-4 and/or .alpha.4.beta.7, and are useful for inhibition or prevention of cell adhesion and cell adhesion

mediated pathologies. These compds. may be formulated into pharmaceutical compns. and are suitable for use in the treatment of asthma, allergies, inflammation, multiple sclerosis, and other inflammatory and autoimmune disorders. Thus, coupling of L-2-naphthylalanine tert-Bu ester (H-Nal-OtBu) (prepn. given) with Cbz-Pro-OH (Cbz = PhCH2O2C), followed by catalytic deprotection, sulfonylation with 3,5-Cl2C6H3SO2Cl, and acidic deesterification gave desired N-sulfonyldipeptide Cl2C6H3SO2-Nal-Pro-OH. Procedures for inhibition of VLA-4 dependent adhesion to a CS-1 conjugate and VCAM-IG fusion protein are given.

IT **217450-85-6P 217452-16-9P 217453-19-5P**
217453-20-8P 217453-22-0P 217453-24-2P
217453-30-0P 217453-31-1P 217453-32-2P
217453-33-3P 217453-34-4P 217453-35-5P
217453-36-6P 217453-37-7P 217453-38-8P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of heterocyclic dipeptide derivs. as cell adhesion inhibitors)

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=> fil caold

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FILE LAST UPDATED: 01 May 1997 (19970501/UP)

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This file supports REG1stRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

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DICTIONARY FILE UPDATES: 07 DEC 99 HIGHEST RN 250252-89-2

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POTENTIAL STEREO BOND SEARCH PROBLEM WITH STN EXPRESS WITH DISCOVER! 5.0 (Windows Only) SEE NEWS 9 FOR DETAILS

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214	RN	217450-85-6	REGISTRY

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RN 220605-30-1 REGISTRY
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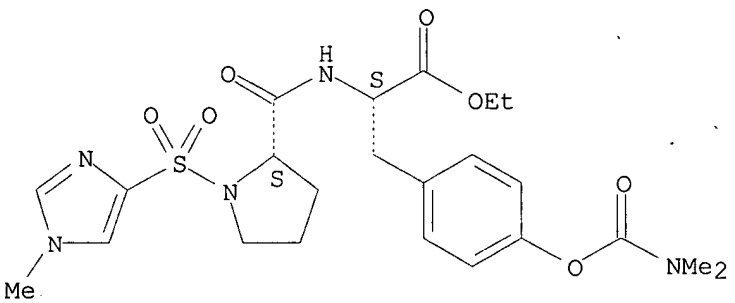
SR CA
LC STN Files: CA, CAPLUS, TOXLIT

Absolute stereochemistry.



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 130:177528

L3 ANSWER 2 OF 214 REGISTRY COPYRIGHT 1999 ACS
RN 220551-47-3 REGISTRY
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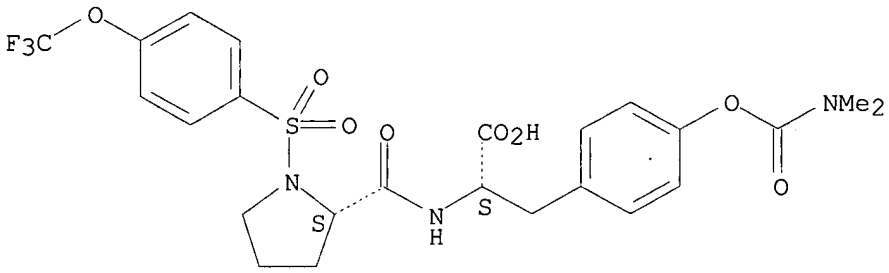
FS STEREOSEARCH
MF C24 H26 F3 N3 O8 S
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 130:182768

L3 ANSWER 4 OF 214 REGISTRY COPYRIGHT 1999 ACS
RN 220548-09-4 REGISTRY
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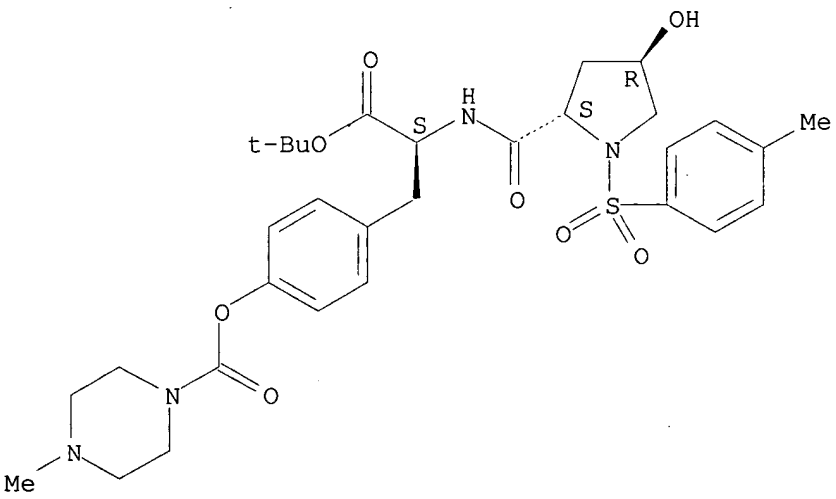
MF C31 H42 N4 O8 S
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 130:182768

L3 ANSWER 6 OF 214 REGISTRY COPYRIGHT 1999 ACS
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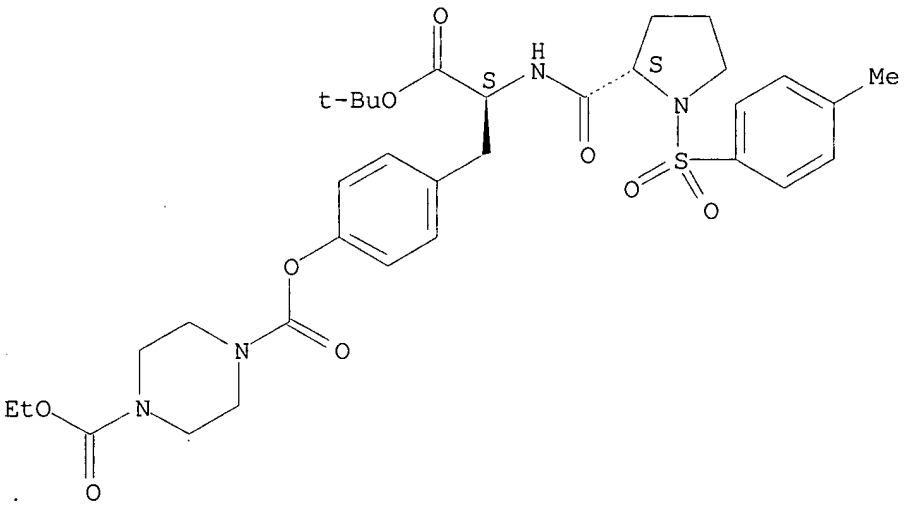
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



1 REFERENCES IN FILE CA (1967 TO DATE)
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REFERENCE 1: 130:182768

L3 ANSWER 53 OF 214 REGISTRY COPYRIGHT 1999 ACS
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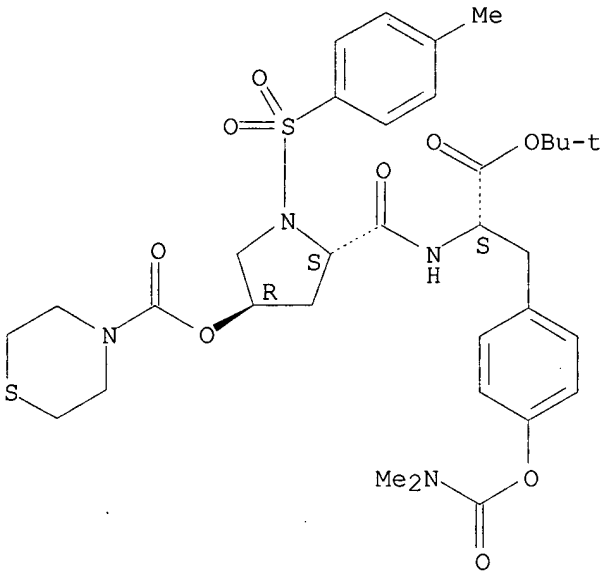
Absolute stereochemistry.



1 REFERENCES IN FILE CA (1967 TO DATE)
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REFERENCE 1: 130:182768

L3 ANSWER 60 OF 214 REGISTRY COPYRIGHT 1999 ACS
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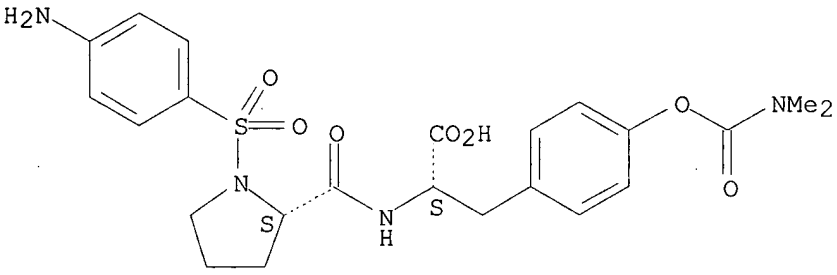
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 130:182768

L3 ANSWER 70 OF 214 REGISTRY COPYRIGHT 1999 ACS
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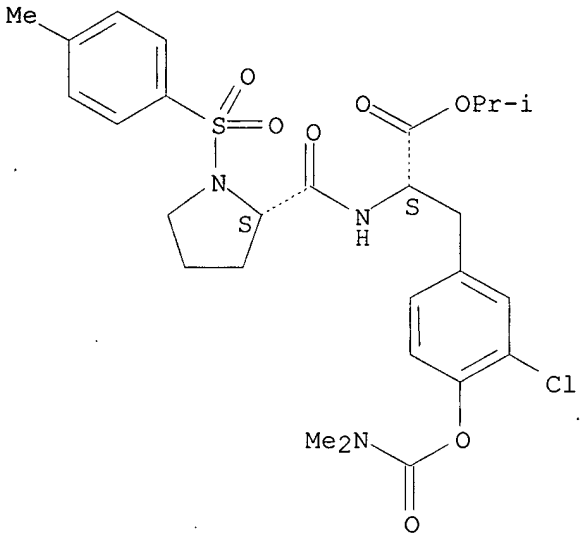
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



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REFERENCE 1: 130:182768

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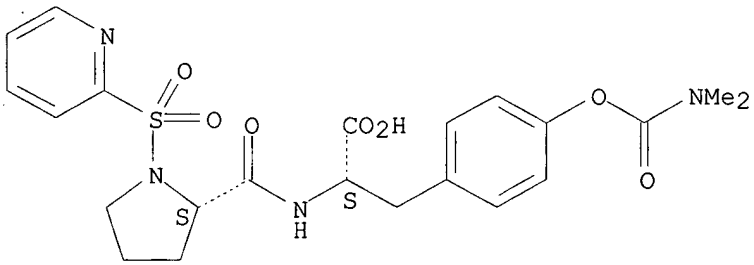
Absolute stereochemistry.



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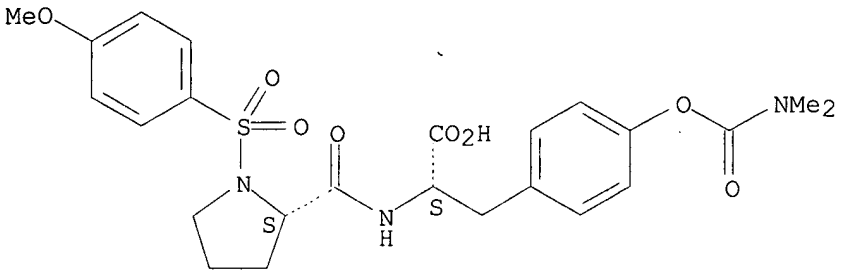
CN L-Tyrosine, 1-[(4-methoxyphenyl)sulfonyl]-L-prolyl-, dimethylcarbamate (ester) (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C24 H29 N3 O8 S
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

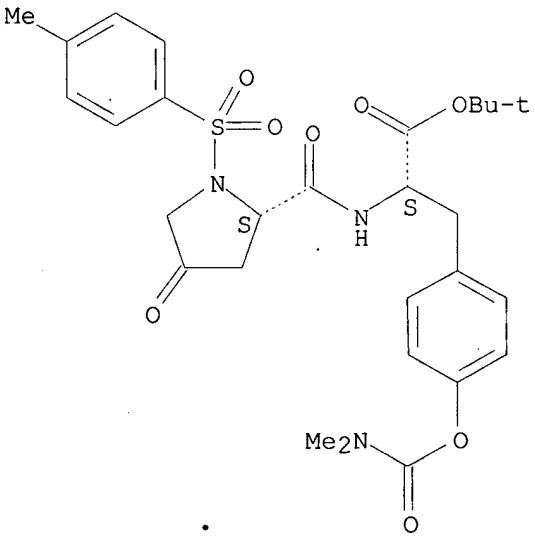


1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 130:182768

L3 ANSWER 96 OF 214 REGISTRY COPYRIGHT 1999 ACS
RN 220545-51-7 REGISTRY
CN L-Tyrosine, 1-[(4-methylphenyl)sulfonyl]-4-oxo-L-prolyl-, 1,1-dimethylethyl ester, dimethylcarbamate (ester) (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C28 H35 N3 O8 S
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



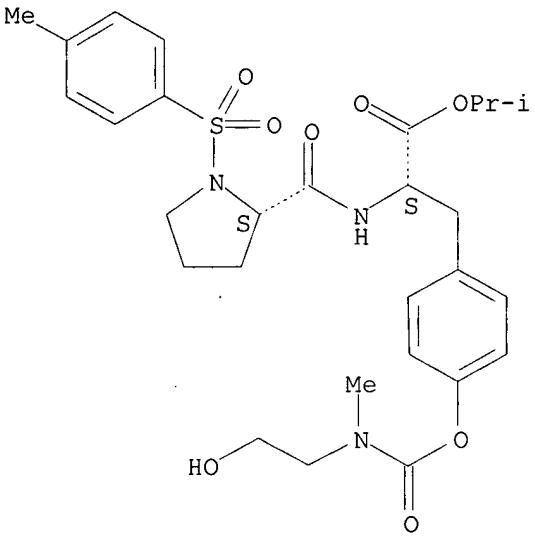
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 130:182768

L3 ANSWER 100 OF 214 REGISTRY COPYRIGHT 1999 ACS
RN 220545-46-0 REGISTRY
CN L-Tyrosine, 1-[(4-methylphenyl)sulfonyl]-L-prolyl-, 1-methylethyl ester, (2-hydroxyethyl)methylcarbamate (ester) (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C28 H37 N3 O8 S
SR CA

LC STN Files: CA, CAPLUS

Absolute stereochemistry.

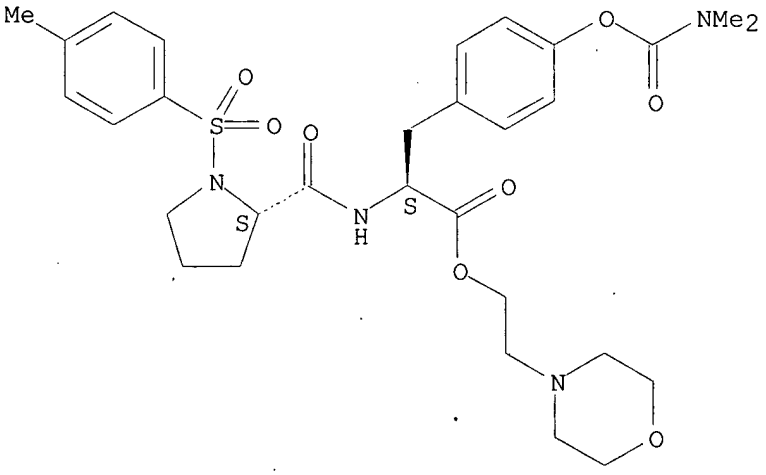


1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 130:182768

L3 ANSWER 110 OF 214 REGISTRY COPYRIGHT 1999 ACS
RN 220545-34-6 REGISTRY
CN L-Tyrosine, 1-[(4-methylphenyl)sulfonyl]-L-prolyl-, 2-(4-morpholinyl)ethyl ester, dimethylcarbamate (ester) (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C30 H40 N4 O8 S
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

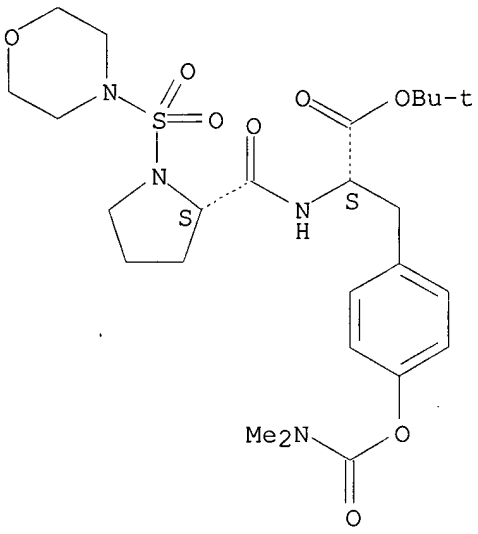


1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 130:182768

L3 ANSWER 120 OF 214 REGISTRY COPYRIGHT 1999 ACS
RN 220545-22-2 REGISTRY
CN L-Tyrosine, 1-(4-morpholinylsulfonyl)-L-prolyl-, 1,1-dimethylethyl ester, dimethylcarbamate (ester) (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C25 H38 N4 O8 S
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

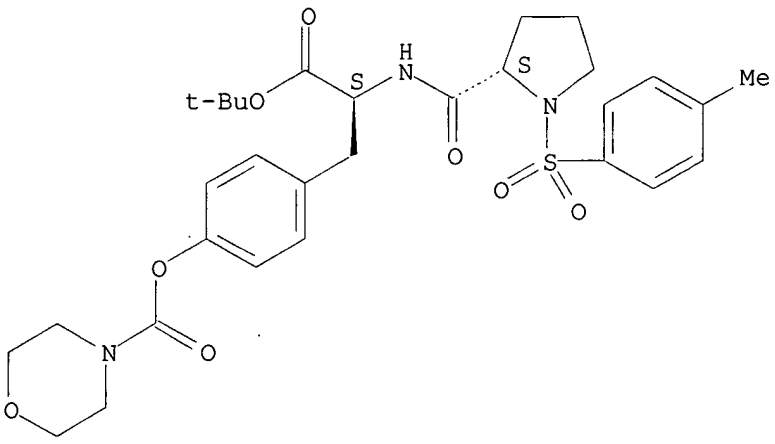


1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 130:182768

L3 ANSWER 138 OF 214 REGISTRY COPYRIGHT 1999 ACS
RN 220544-94-5 REGISTRY
CN L-Tyrosine, 1-[(4-methylphenyl)sulfonyl]-L-prolyl-, 1,1-dimethylethyl ester, 4-morpholinecarboxylate (ester) (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C30 H39 N3 O8 S
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

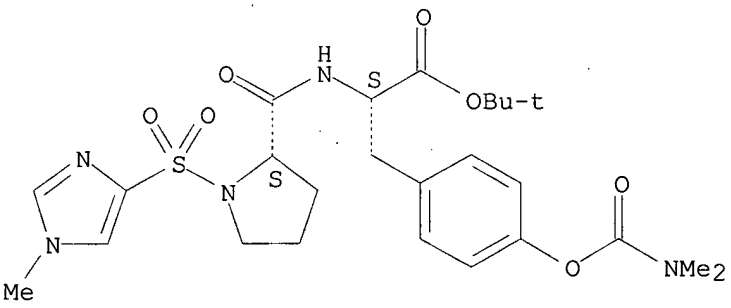


1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 130:182768

L3 ANSWER 140 OF 214 REGISTRY COPYRIGHT 1999 ACS
RN 220544-90-1 REGISTRY
CN L-Tyrosine, 1-[(1-methyl-1H-imidazol-4-yl)sulfonyl]-L-prolyl-, 1,1-dimethylethyl ester, dimethylcarbamate (ester) (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C25 H35 N5 O7 S
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

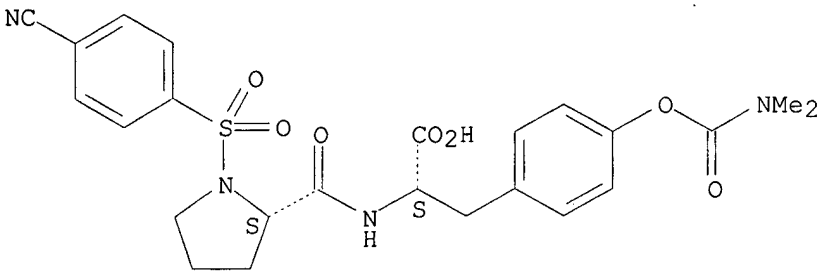


1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 130:182768

L3 ANSWER 150 OF 214 REGISTRY COPYRIGHT 1999 ACS
RN 220544-79-6 REGISTRY
CN L-Tyrosine, 1-[(4-cyanophenyl)sulfonyl]-L-prolyl-, dimethylcarbamate (ester) (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C24 H26 N4 O7 S
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

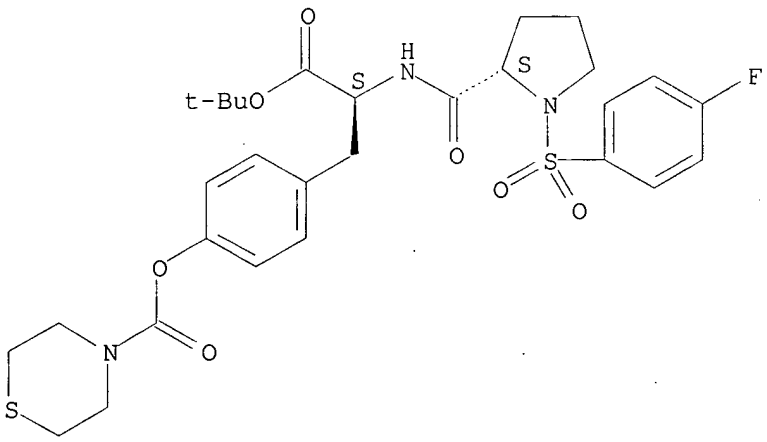


1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 130:182768

L3 ANSWER 160 OF 214 REGISTRY COPYRIGHT 1999 ACS
RN 220544-55-8 REGISTRY
CN L-Tyrosine, 1-[(4-fluorophenyl)sulfonyl]-L-prolyl-, 1,1-dimethylethyl ester, 4-thiomorpholinecarboxylate (ester) (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C29 H36 F N3 O7 S2
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

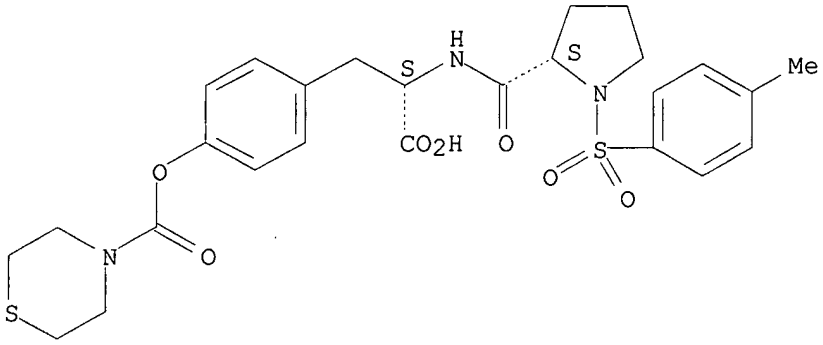


1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 130:182768

L3 ANSWER 170 OF 214 REGISTRY COPYRIGHT 1999 ACS
RN 220544-32-1 REGISTRY
CN L-Tyrosine, 1-[(4-methylphenyl)sulfonyl]-L-prolyl-, 4-thiomorpholinecarboxylate (ester) (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C26 H31 N3 O7 S2
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

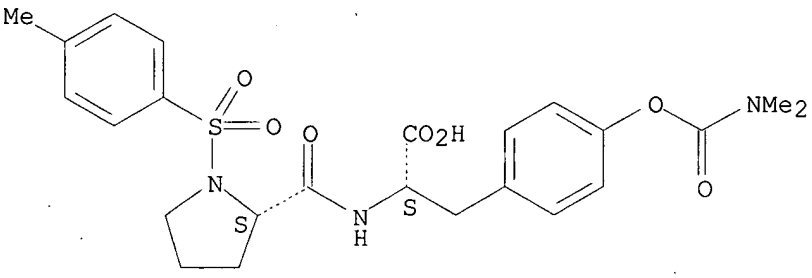


1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 130:182768

L3 ANSWER 179 OF 214 REGISTRY COPYRIGHT 1999 ACS
RN 220543-99-7 REGISTRY
CN L-Tyrosine, 1-[(4-methylphenyl)sulfonyl]-L-prolyl-, dimethylcarbamate (ester) (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C24 H29 N3 O7 S
SR CA
LC STN Files: CA, CAPLUS, TOXLIT

Absolute stereochemistry.



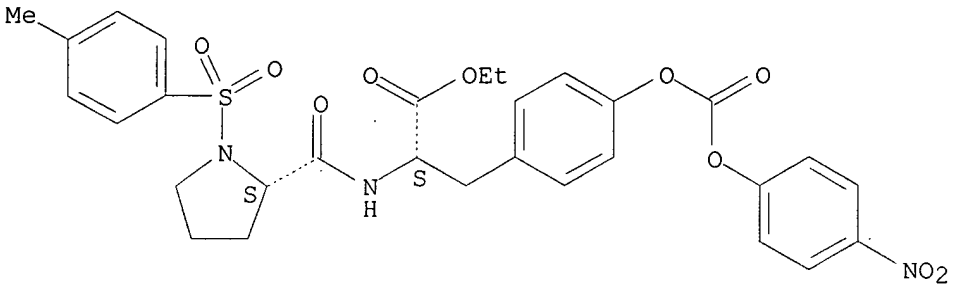
2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 130:182768

REFERENCE 2: 130:177528

L3 ANSWER 188 OF 214 REGISTRY COPYRIGHT 1999 ACS
RN 220303-19-5 REGISTRY
CN L-Tyrosine, 1-[(4-methylphenyl)sulfonyl]-L-prolyl-, ethyl ester, 4-nitrophenyl carbonate (ester) (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C30 H31 N3 O10 S
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

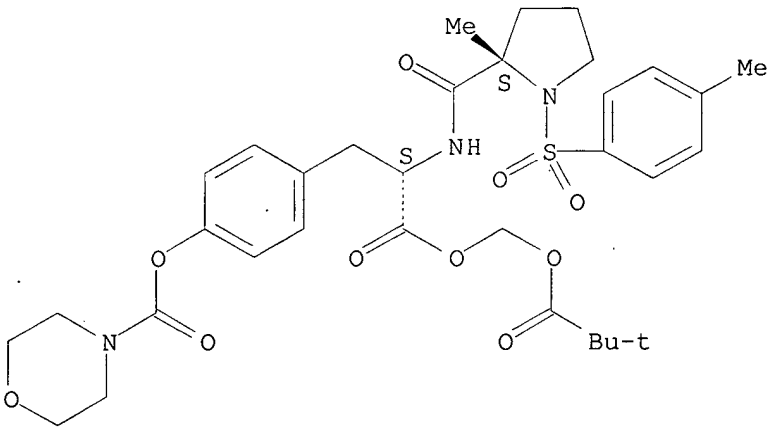


1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 130:168662

L3 ANSWER 189 OF 214 REGISTRY COPYRIGHT 1999 ACS
RN 220173-47-7 REGISTRY
CN L-Tyrosine, 2-methyl-1-[(4-methylphenyl)sulfonyl]-L-prolyl-, (2,2-dimethyl-1-oxopropoxy)methyl ester, 4-morpholinecarboxylate (ester) (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C33 H43 N3 O10 S
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

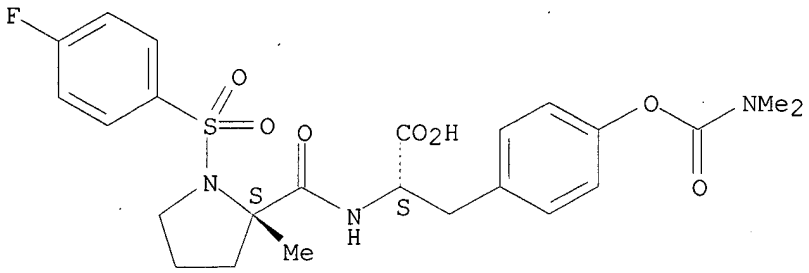


1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 130:153984

L3 ANSWER 196 OF 214 REGISTRY COPYRIGHT 1999 ACS
RN 220172-92-9 REGISTRY
CN L-Tyrosine, 1-[(4-fluorophenyl)sulfonyl]-2-methyl-L-prolyl-, dimethylcarbamate (ester) (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C24 H28 F N3 O7 S
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

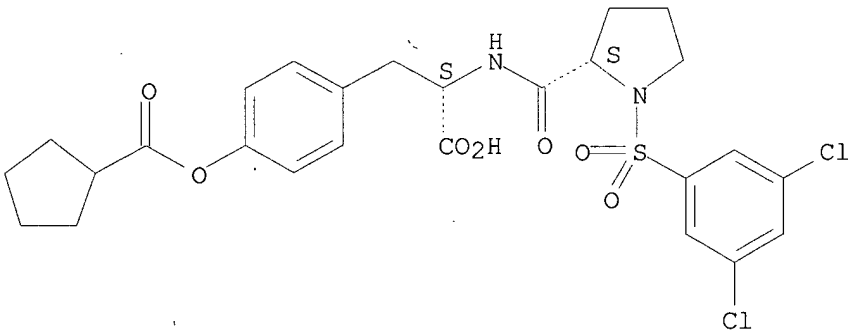


1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 130:153984

L3 ANSWER 200 OF 214 REGISTRY COPYRIGHT 1999 ACS
RN 217453-38-8 REGISTRY
CN L-Tyrosine, 1-[(3,5-dichlorophenyl)sulfonyl]-L-prolyl-, cyclopentanecarboxylate (ester) (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C26 H28 Cl2 N2 O7 S
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

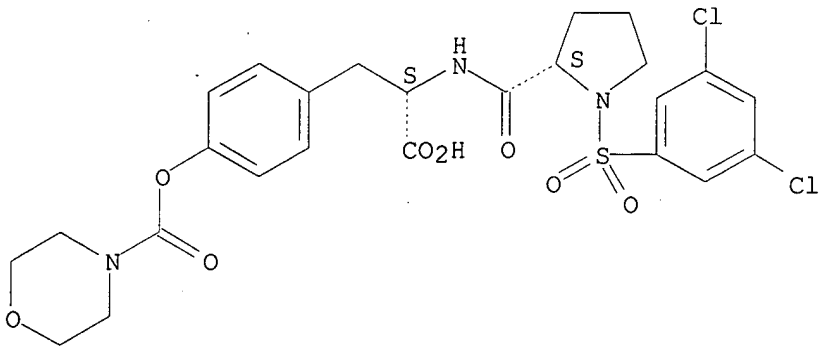


1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 130:52724

L3 ANSWER 210 OF 214 REGISTRY COPYRIGHT 1999 ACS
RN 217453-22-0 REGISTRY
CN L-Tyrosine, 1-[(3,5-dichlorophenyl)sulfonyl]-L-prolyl-, 4-morpholinecarboxylate (ester) (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C25 H27 Cl2 N3 O8 S
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

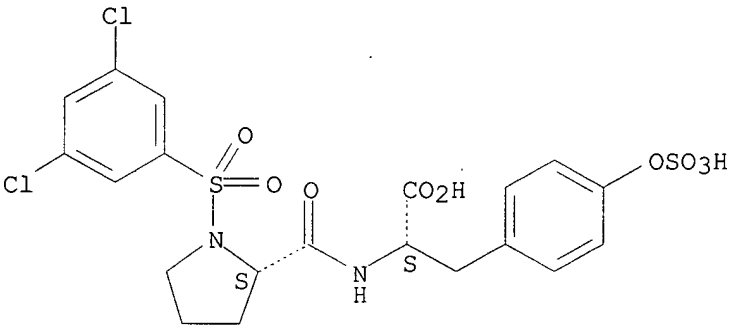


1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 130:52724

L3 ANSWER 214 OF 214 REGISTRY COPYRIGHT 1999 ACS
RN 217450-85-6 REGISTRY
CN L-Tyrosine, 1-[(3,5-dichlorophenyl)sulfonyl]-L-prolyl-, hydrogen sulfate (ester) (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C20 H20 Cl2 N2 O9 S2
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 130:52724